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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/454,223	12/09/1999	RICHARD S. KORNBLUTH	SD9-003-1	3505

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EXAMINER

SEHARASEYON, JEGATHEESAN

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/454,223	KORNBLUTH, RICHARD S.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 February 2005 and 31 March 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7 and 16-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7 and 16-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>3/14/04 & 2/28/05</u> <i>CP</i> | 6) <input type="checkbox"/> Other: _____ |

Handwritten initials

DETAILED ACTION

1. This office action is in response to claims and preliminary amendment provided 2/28/05 and 3/31/2005. Claim 8 has been cancelled. Claim 7 has been amended. Claims 16-28 have been added. Therefore, claims 7 and 16-28 are pending.
2. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

Specification

3. The corrections to the disclosure are acknowledged.
4. Sequence compliance is also acknowledged.

Information Disclosure Statement

5. The Office acknowledges the submission of IDS on 3/14/04 and 2/28/05
6. The notes a typographical error of not adding claim 7 on paragraph 6a, line 1. The body of the rejection does recite both the claims.
7. Claim rejections necessitated by Applicants amendments and addition new claims.

Claim Rejections - 35 USC § 112, second paragraph, maintained

8. Claims 7 and 16-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
- 8a. Claim 7 is rejected as being vague and indefinite in the recitation of the term "TNFSF polypeptide". It is unclear which TNFSF polypeptides are encompassed in the instant claim. Therefore, the metes and bounds of the claim are unclear. Claims 16-28 are rejected insofar as it depends on rejected claim 7.

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8b. Claims 16 and 17 are rejected as being vague and indefinite in the recitation of the term "functional equivalents". It is unclear which functional equivalents are encompassed in the instant claims.

8c. Claims 17, 21 and 23 are rejected as vague and indefinite for reciting the terms C1q, MBL1, MBL2, CL-L1, ACRP30, Hib27 and RANKL, because the full meaning of an acronym should be spelled out at its first use in the claims.

Claim Rejections - 35 USC § 112, first paragraph, maintained

9a. Claims 7, 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses the human and murine CD40L, T147N modification of CD40L and RANKL/TRANCE polypeptides (page: 21, line 18 to page: 24, line 2). This meets the written description and enablement provisions of 35 USC 112, first paragraph. However, the specification does not disclose polypeptide sequences of the other TNFSF proteins and functional equivalents thereof. Also they do not describe the various trimer units that will be linked to the TNFSF. The claims as written, however, encompass polypeptide sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 7, 16 and

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17. The specification does not provide written support to the genus encompassed by the instant claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed” (See *Vas-Cath* at page 1116).

With the exception of the polypeptides CD40L, T147N modification of CD40L and RANKL/TRANCE, the skilled artisan cannot envision all the detailed chemical structure of the claimed polypeptides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required.

See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF’s were found unpatentable due to lack of written description for the broad class.

Therefore, only the polypeptides CD40L, T147N modification of CD40L and RANKL/TRANCE, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of various polypeptide sequences set forth in claims 7, 16 and 17.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

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Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

9b. Claims 7, 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for CD40L-SPD, T146N-CD40L-SPD and RANKL/TRANCE-SPD fusion protein does not reasonably provide enablement for other fusion polypeptides consisting of TNFSF functional equivalents, and modifications thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

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The instant claims read on all TNFSF multimeric polypeptides that contain at least a dimer of trimer units. However, other than CD40L-SPD, T147N-CD40L-SPD and RANKL/TRANSE -SPD fusion polypeptide, the specification as filed fails to disclose any other fusion polypeptide.

Despite knowledge in the art for producing multimeric fusion proteins specification fails to provide any guidance regarding the generation of the fusion proteins and yet retain the function. Furthermore, detailed information regarding the structural and functional requirements of the disclosed protein is lacking. Although it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. Therefore, predicting which TNFSF multimeric fusion polypeptides or functional equivalents would retain the functions of the protein is well outside the realm of routine experimentation. Thus, undue amount of experimentation would be required to generate changes/modifications contemplated and yet retain the function of the proteins claimed.

Applicants have not taught how one of skill in the art would use the full scope of fusion proteins encompassed by the invention of claims. The specification as filed does not sufficiently teach one of skill in the art how to make and/or use the full scope of the claimed polypeptides. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the functional sequences. Given the breadth of claims 7, 16 and 17 in light of the unpredictability of the art as determined by the lack of working examples and shown

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by the prior art of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

10. No claims are allowable but they are apparently free of prior art.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSS 06/05


JANET ANDRES
PRIMARY EXAMINER